other lipoproteins, LpX migrates toward the cathode in agarose gel, making it easy to distinguish from other lipoproteins.

Currently, one FDA-approved polyacrylamide tube gel electrophoresis system is available for separating LDL into seven subfractions: the LipoPrint system from Quantimetrix (6). As will be discussed further, researchers have found that small dense LDL subfractions are more closely related to CVD risk than LDL-C, most likely because of their increased ability to enter atherosclerotic plaques. Certain reference labs offer 2D-gel electrophoresis tests that separate HDL into at least five subfractions, and may also measure the amount of apolipoprotein A-I (apoA-I) in each of the five HDL subclasses (7).

**DENSITY-GRADIENT ULTRACENTRIFUGATION**

Density-gradient ultracentrifugation involves separating lipoproteins according to their density and depends on the lipid/protein ratio of lipoproteins. Chylomicrons, for example, are almost completely comprised of lipids and are very light, with a density less than water. In contrast, the smaller lipoproteins, such as HDL, are only about 50% by weight lipids with the other half made up of denser proteins, giving HDL a density range between 1.063–1.25 g/mL. Density-gradient ultracentrifugation not only forms the basis for the main nomenclature of lipoproteins but also serves as a reference method for measuring lipoproteins (8). Even these subfractions. The test measures IDL-C and Lp(a)-C using software that deconvolutes data embedded in the parent tracing. It also assesses total cholesterol, triglycerides, the main protein components of HDL and LDL, apoA-I, and apolipoprotein B (apoB), respectively, which can be used to estimate the particle number of these lipoproteins. VAP classifies LDL subfractions as “pattern A,” “pattern B,” or “pattern A/B.” “Pattern A” implies large, buoyant LDL particles, whereas “pattern B” implies small, dense LDL particles (Table 2), which have been strongly associated with CVD risk. The test also separates cholesterol on HDL into a larger, less dense HDL subclass (HDL₃) and small, denser HDL subclass (HDL₂) (9). Although the clinical utility for HDL subfractions is not as large size—can be easily observed in agarose gels because they stay trapped near the origin of the gel. In contrast, VLDL, the only other particle that carries significant amounts of triglycerides, migrates much further into the gel (Fig. 1). Patients with dysbetalipoproteinemia have a defect in the clearance of chylomicrons and VLDL and accumulate intermediate density lipoproteins (IDL), often referred to as remnant lipoproteins. These tend to migrate between LDL and VLDL on agarose gels. Dysbetalipoproteinemia is a relatively common disorder that affects about 1% of the population. Identifying individuals with this condition is important because they might benefit from both statins and drugs that specifically lower triglycerides.

Agarose gel electrophoresis is also one of the few methods available for detecting lipoprotein X (LpX), an abnormal lipoprotein particle that accumulates in patients with cholestasis and familial lecithin-cholesterol acyltransferase deficiency. Unlike other lipoproteins, LpX migrates as remnant lipoproteins. These tend to migrate between LDL and VLDL on agarose gels. Dysbetalipoproteinemia is a relatively common disorder that affects about 1% of the population. Identifying individuals with this condition is important because they might benefit from both statins and drugs that specifically lower triglycerides.

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